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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/967,237	ZAVADA ET AL.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-27 and 30-52* is/are pending in the application.

4a) Of the above claim(s) *24-27,32-35,39-41,44,45 and 49-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,23,30,31,36-38,42-43,46-48 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/19/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 22-23, 30-31, 36-38, 42-43, 46-48 and 52 in the Paper filed 1/5/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 32-35, 39-41, 44-45 and 49-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Specification

3. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

5. The use of the trademark ® has been noted in this application. See page 48, 57, 58 or 100, for example. Trademarks should be capitalized or accompanied by the ® or ™ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary

nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 22-23, 30-31, 36-38, 42-43 and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 22-23, 30-31, 36-38, 42-43 and 46-48 are indefinite for reciting "hybridize under stringent conditions" in claim 22, 30 and 42 because the exact meaning of the phase is not clear. It is not clear what full set of conditions is encompassed in the claims. The specification discloses several conditions on page 60 as well as "less stringent" and "more stringent" and it is not clear which if any of these conditions are required for the claims.

b. Claim 37 recites the limitation " said polynucleotide ". There is insufficient antecedent basis for this limitation in the claim. It is unclear which polynucleotide recited in the parent claim (claim 30) is required by dependent claim 37.

c. Claims 47-48 are indefinite for reciting "fragment of SEQ ID NO:1". Claim 30 from which claim 47 depends recites that the MN polypeptide is encoded by a polynucleotide containing at least 29 nucleotides of SEQ ID NO:1 and claim 42 from

which claim 48 depends, recites that the MN polypeptide is encoded by a polynucleotide containing at least 25 nucleotides of SEQ ID NO:1. Thus, it is unclear if the "fragment of SEQ ID NO:1" is a fragment of the full-length SEQ ID NO:1 or is the "fragment of SEQ ID NO:1" a fragment of the polynucleotide portions (i.e., 29 and 25 nucleotides of SEQ ID NO:1) of SEQ ID NO:1?

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 30-31, 36-38, 42-43, 46-48 and 52are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Newly added claims recite limitations of an anti-idiotype antibody that binds to an antibody that specifically binds to an MN polypeptide that is encoded by a polynucleotide that comprises a certain number of nucleotides of SEQ ID NO:1 or the MN protein or polypeptide is encoded by a fragment of SEQ ID NO:1 and claim 52 recites the stringent hybridization conditions.

The preliminary amendment filed 9/27/2001 pointed to the specification where support can be found for the newly added claims, however, support for the instant claim limitations can not apparently be found. Support for claims reciting an anti-idiotype antibody that binds to an antibody that specifically binds to an MN polypeptide that is encoded by a polynucleotide that comprises a certain number of nucleotides of SEQ ID NO:1 is not supported by the disclosure pointed to by applicant on pages 8-9 and at page 60 because the disclosure on these pages only provides support for nucleic acid probes comprising "a polynucleotide containing different numbers of nucleotides." Although the polynucelotides are disclosed as encoding MN proteins or polypeptides there is apparently no support for an antibody that binds said MN proteins or polypeptides, much less an anti-idiotype antibody to the antibody, which binds said MN proteins or polypeptides. Additionally, there is no apparent support for claims 46-49, which recite the broad limitation of an anti-idiotype antibody to an antibody that binds an MN protein or polypeptide wherein the MN protein or polypeptide is encoded by any fragment of SEQ ID NO:1. Similarly, the disclosure of the stringent hybridization conditions (recited in newly added claim 52) as found at page 7, lines 16-18 and page 8, lines 12-14, in the context of nucleic acid probes does not adequately provide support for an anti-idiotypic antibody to an antibody that specifically binds an MN protein or polypeptide that is encoded by a polynucleotide that hybridizes to the complement of SEQ ID NO:1 under said stringent hybridization conditions. Applicant is required to specifically point out where support for all of the newly added claim limitations can be

found in the originally filed specification or claims or remove these limitations from the claims.

10. Claims 22, 30, 36-38, 42-43 and 46-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a anti-idiotype antibody type beta ($Ab_2\beta$; binds to the CDR and is an internal image of the antigen) to monoclonal antibodies (Mabs) M75, MN9, MN12, MN7 and G250 that specifically bind SEQ ID NO:2 (i.e., the MN protein encoded by SEQ ID NO:1 or the polynucleotide portions thereof or by polynucleotides that differ from SEQ ID NO:1 or differ from the polynucleotides that hybridize under stringent conditions to the complement of SEQ ID NO:1 due to the degeneracy of the genetic code), does not reasonably provide enablement for just any anti-idiotypic (i.e., -alpha ($Ab_2\alpha$) or -epsilon ($Ab_2\varepsilon$)) antibody that binds just any antibody that binds to an MN protein encoded by SEQ ID NO:1 or just any fragment of SEQ ID NO:1 that does not encode an epitope recognized by Mabs M75, MN9, MN12, MN7 and G250 or an MN protein/polypeptide encoded by polynucleotides that hybridize under stringent conditions to the complement of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in

the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to any anti-idiotypic antibody to any antibody that binds to any MN protein or binds just any MN polypeptide fragment encoded by polynucleotide portions of SEQ ID NO:1, or polynucleotides that hybridize under stringent conditions to the complement of SEQ ID NO:1 or polynucleotides that differ from SEQ ID NO:1 or differ from polynucleotides that hybridize under stringent conditions to the complement of SEQ ID NO:1 due to the degeneracy of the genetic code.

The specification does not disclose any working examples of an anti-idiotype antibody to an antibody that binds an MN protein, however, the specification discloses several monoclonal antibodies, Mab M75, Mab MN9, Mab MN12, Mab MN7 and Mab G250, which specifically bind the MN protein. The specification further discloses the binding sites or epitopes of Mabs M75, MN9, MN12 and MN7, all of which bind specific epitopes in the proteoglycan domain (PG) (see pages 72-73 and Figure 8) except Mab MN7, which binds an epitope corresponding to amino acids 127-147 of SEQ ID NO:1 (see page 73 and Figures 1 and 8). The binding site of Mab M75 was shown to be closely related or identical to the cell-adhesion binding site of MN (see Example 4) and Mab MN9 recognizes the same epitope as Mab M75 (see page 73, lines 13-14). The MN protein is a cell surface protein and is a tumor-associated cell adhesion molecule.

The G250 antigen recognized by Mab G250 was shown to be identical to the MN protein, a human tumor-associated antigen (see page 3, lines 26-31).

The claims encompass anti-idiotypic antibodies that bind to any antibody that binds anywhere on an MN protein encoded by SEQ ID NO:1 or encoded by fragments of SEQ ID NO:1 or encoded by polynucleotides that hybridize under stringent conditions to the complement of SEQ ID NO:1 or polynucleotides that differ from SEQ ID NO:1 or differ from the polynucleotides that hybridize under stringent conditions to the complement of SEQ ID NO:1 due to the degeneracy of the genetic code. The art teaches that the process of generating internal image anti-idiotype antibodies are well known to those of skill in the art and can result in the production of internal image antibodies that mimic the immunological properties of the initial antigen (i.e., tumor antigen or infectious agent). For support, see Raychaudhuri S., U.S. Patent 5,270,202, bridging paragraph of columns 2-3). Wu, X-R (U.S. Patent 6,632,431 B2) teaches the three types of anti-idiotypic antibodies, alpha ($Ab_2\alpha$), beta ($Ab_2\beta$) and epsilon ($Ab_2\varepsilon$) and only $Ab_2\beta$, which binds to the CDR can be an internal image of the antigen and has been proposed to be paratropic and to mimic the molecular features of the original antigen (see column 3, lines 44-58). Raychaudhuri S. acknowledges that the successful production of anti-idiotypic antibodies is an unpredictable endeavor (see column 3, lines 35-54). "In short, the discovery of therapeutically useful anti-idiotypic antibodies is as much art as science" (see column 3, lines 49-51). Chatterjee et al (U.S. Patent 6,235,280 B1) teach that not all anti-idiotype antibodies can be used in therapeutic regimens against tumors. First, only a fraction of antibodies raised against

an Ab1 (anti-antigen antibody) are limited in their reactivity to the paratope of Ab1 (i.e., are non-reactive against features shared with other potential antibodies in the host). Second, anti-idiotype antibodies are not necessarily immunogenic. Third, only a fraction of the immunogenic anti-idiotypes elicit an antigen-specific immune response. Further, anti-idiotype therapy with respect to tumor origin and antigens expressed should be evaluated on a case-by-case basis since different cancers have widely varying molecular and clinical characteristics (see column 2, lines 39-53).

The claims are broad because they do not require that the claimed polynucleotides and the encoded polypeptides to be identical to the disclosed MN sequences (i.e., SEQ ID Nos. 1 and 2) and because the claims have no functional limitation. The claims also encompass polynucleotides and polynucleotide fragments that hybridize to the complement of SEQ ID NO:1 under stringent conditions, however, the claims do not recite under what full set of conditions are used for hybridization or if the polynucleotides hybridize to the full length of SEQ ID NO:1 or if the hybridized polynucleotides encode a polypeptide of SEQ ID NO:2 (i.e., the disclosed MN polypeptide). Even if the claimed polynucleotides and polypeptides encoded thereby had a function the specification does not provide guidance for using polynucleotides related to (see page 52), but not identical to SEQ ID NO:1 or polypeptides related to, but not identical to the polypeptide of SEQ ID NO:2.

Applicants have provided insufficient evidence or nexus that would lead the skilled artisan to predict the ability to use just any anti-idiotypic antibody to just any antibody that binds to an MN protein or binds just any MN polypeptide fragment

encoded by polynucleotides of SEQ ID NO:1, or polynucleotides that hybridize under stringent conditions to the complement of SEQ ID NO:1 or polynucleotides that differ from SEQ ID NO:1 or differ from polynucleotides that hybridize under stringent conditions to the complement of SEQ ID NO:1 wherein the polynucleotides do not encode the protein or a polypeptide of SEQ ID NO:2 (i.e., the MN protein/polypeptide). One of skill in the art would neither expect nor predict the appropriate functioning of the anti-idiotypic antibodies as broadly as is claimed.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to any anti-idiotypic antibody to any antibody that binds to an MN protein or an MN polypeptide fragment that is not identical to SEQ ID NO:2.

11. Claims 23 and 31 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line, which produces an antibody having the exact chemical identity of antibody M75 and MN12 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell

line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d Ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species antibody M75 and MN12.

The specification lacks complete deposit information for the deposit of anti-MN antibodies M75 and MN12. It is unclear whether antibodies possessing the identical properties of antibody M75 or MN12 are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce antibodies and hybridomas which are chemically and structurally identical to those claimed. It is

unclear that one of skill in the art could derive a monoclonal antibody and hybridoma identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed antibodies M75 and MN12, a suitable deposit is required for patent purposes, evidence of public availability of the claimed antibody or evidence of the reproducibility without undue experimentation of the claimed antibody, is required.

Applicant's referral to the deposit of the instantly claimed hybridomas of VU-M75 and MN 12.2.2 as ATCC No. HB 11128 and ATCC No. HB 11647 respectively, on page 117 of the specification is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of hybridomas VU-M75 and MN 12.2.2, which produce antibodies M75 and MN12 respectively, has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when

deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit of hybridomas VU-M75 and MN 12.2.2, which produce antibodies M75 and MN12 respectively is not made under the provisions of the Budapest Treaty, then in order to certify that the deposit complies with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed. As indicated above, a verified statement is required for hybridoma MN 12.2.2, which produces antibody MN12 because hybridoma MN 12.2.2 was deposited on 6/9/1994 and the effective filing date of the instant application is deemed to be 12/30/1993.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Priority

12. The filing date of the instant claims is deemed to be the filing date of parent application USSN 08/177,093, i.e., 12/30/1993 (now U.S. Patent 6,051,226). It is noted that priority application Czechoslovakian patent Application PV-709-92; filed 3/11/1992

is not available to the examiner at this time. Priority application USSN 07/964,589 (now U.S. Patent 5,387,676) does not apparently support the claims of the instant application. The MN sequence (cDNA and amino acid sequence) disclosed in U.S. Patent 5,387,676 (i.e., USSN 07/964,589) (see Figure 1A-B) diverges from the instantly claimed MN sequence (cDNA and amino acid sequence) beginning at amino acid residue 411 (see Figure 1B) (compare Figure 1B, residues 411-429 of U.S. Patent 5,387,676 to Figure 1C, residues 449-459 of the instant disclosure).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 22-23, 30-31, 36-38, 42-43, 46-48 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pastorekova et al (Virology, 187:620-626, 3/9/1992, Ids 10/19/2001) as evidenced by Pastorek et al (Oncogene, 9:2877-2888, 1994, Ids 10/19/2001) in view of Raychaudhuri et al (The Journal of Immunology, 13(5):1743-1749, 1986).

The claims are drawn to an anti-idiotypic antibody to an antibody which specifically binds an MN protein encoded by SEQ ID NO:1 or encoded by polynucleotides that hybridize under stringent conditions, which comprise 50% formamide at 42°C, wherein the anti-MN antibody is the M75 monoclonal antibody (Mab). The claims reciting a nucleic acid that comprises a polynucleotide of at least a certain number of nucleotides that encodes an MN protein or polypeptide or fragments of SEQ ID NO:1 encoding the MN protein or polypeptide are reasonably interpreted to comprise the MN epitope recognized by Mab M75.

Pastorekova et al teach that the MN protein is one part of a two-part agent, MaTu. Pastorekova et al teach the M75 monoclonal antibody, which reacts with two MN-specific protein bands of 54K and 58K, which are presumed to represent different glycoforms of the same polypeptide (see Figures 3 and 5 and page 621, right column and page 625, right column). As evidence by Pastorek et al the MN polypeptides (i.e., the 54 and 58kDa; see Figure 4) with which Mab M75 reacts share 100% amino acid identity with the disclosed MN polypeptide of SEQ ID NO:2 (see the sequence alignment attached to the back of this office action), which is encoded by SEQ ID NO:1. Pastorekova et al also teach that MaTu is a quasi-viral agent derived from a human

mammary tumor and MN is the endogenous, inducible component of the MaTu system and MN is actually the donor of the envelope proteins for vesicular stomatitis virus pseudotype virions (VSV) (see abstract and page 620, right column) and MN antigens are expressed in the nucleus and in the cell surface membrane (see Figures 1A and 1B). Pastorekova et al do not specifically teach anti-idiotypic antibodies to Mab M75. This deficiency is made up for in the teachings of Raychaudhuri et al.

Raychaudhuri et al teach that immunization with anti-idiotype antibodies of the beta type ($Ab_2\beta$), bearing the internal image of a tumor antigen, induces tumor-specific immunity and can inhibit tumor growth (see Figures 4 and 6 and Table III).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen in view of Pastorekova et al as evidenced by Pastorek et al and in view of Raychaudhuri et al because Pastorekova et al teach that the MN protein is a human tumor-associated antigen expressed on the cell surface and monoclonal antibody M75 specifically reacts with the MN protein which is identical to the MN protein (i.e., SEQ ID NO:2) (see the attached sequence alignment) encoded by SEQ ID NO:1 as evidenced by Pastorek et al. Pastorek et al teach the sequence of the

MN protein (see Figure 1). Furthermore, it would have been obvious to one skilled in the art that the polynucleotide encoding the MN protein, which shares 100% amino acid identity with the MN protein encoded by instantly claimed SEQ ID NO:1 would hybridize to the complement of SEQ ID NO:1 under the claimed stringent conditions. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen in view of Pastorekova et al as evidenced by Pastorek et al in view of Raychaudhuri et al because Raychaudhuri et al teach that immunization with anti-idiotype antibodies of the beta type (i.e., $Ab_2\beta$), bearing the internal image of a tumor antigen, induces tumor-specific immunity and can inhibit tumor growth. Thus, it would have been obvious to one skilled in the art to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen in view of Pastorekova et al as evidenced by Pastorek et al and in view of Raychaudhuri et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

16. Claims 22, 30, 36-38, 42-43, 46-48 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterwijk et al (WO 88/08854, Publication date 11/17/1988, Ids 10/19/2001) as evidenced by Uemura et al (British journal of Cancer,

81(4):741-746, 1999) and Pastorek et al and in view of Raychaudhuri et al (The Journal of Immunology, 139(1):271-278, 1987).

The claims have been described supra.

Oosterwijk et al teach a monoclonal antibody G 250 (Mab G 250) that reacts with a renal cell carcinoma antigen, G 250 antigen (see Examples 3-4). The G 250 antigen was also found in a few benign tumors and premalignant lesions (see pages 5-6 and Figure 4). As evidenced by Uemura et al the G 250 antigen is identical to MN protein (also known as carbonic anhydrase IX; CA IX or CA9) (see page 744, left and right column) and Pastorek et al teach the MN protein sequence, which shares 100% amino acid identity with the disclosed MN polypeptide of SEQ ID NO:2 (see the sequence alignment attached to the back of this office action), which is encoded by SEQ ID NO:1. Oosterwijk et al do not specifically teach an anti-idiotype antibody to an antibody that specifically binds to an MN protein. This deficiency is made up for in the teachings of Raychaudhuri et al.

Raychaudhuri et al has been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human

tumors expressing the MN tumor antigen in view of Oosterwijk et al as evidenced by Uemura et al and Pastorek et al and in view of Raychaudhuri et al because Oosterwijk et al teach monoclonal antibody G 250 (Mab G 250) that reacts with a renal cell carcinoma antigen, the G 250 antigen, which was also found in a few benign tumors and premalignant lesions (see pages 5-6 and Figure 4). As evidenced by Uemura et al the G 250 antigen is identical to MN protein (also known as carbonic anhydrase IX; CA IX or CA9) (see page 744, left and right column) and Pastorek et al teach the MN protein sequence, which shares 100% amino acid identity with the disclosed MN polypeptide of SEQ ID NO:2 (see the sequence alignment attached to the back of this office action), which is encoded by SEQ ID NO:1. Furthermore, it would have been obvious to one skilled in the art that the polynucleotide encoding the MN protein, which shares 100% amino acid identity with the MN protein encoded by instantly claimed SEQ ID NO:1 would hybridize to the complement of SEQ ID NO:1 under the claimed stringent conditions. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen in view of Oosterwijk et al as evidenced by Uemura et al and Pastorek et al in view of Raychaudhuri et al because Raychaudhuri et al teach that immunization with anti-idiotype antibodies of the beta type (i.e., $Ab_2\beta$), bearing the internal image of a tumor antigen, induces tumor-specific immunity and can inhibit tumor growth. Thus, it would have been obvious to one skilled in the art to have produced an anti-idiotype antibody to an antibody that specifically

binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen in view of Oosterwijk et al as evidenced by Uemura et al and Pastorek et al and in view of Raychaudhuri et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

17. Claims 22, 30, 36-38, 42-43, 46-48 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterwijk et al (International Journal of Cancer, 38: 489-494, 1986, Ids 10/19/2001) as evidenced by Uemura et al and Pastorek et al in view of Raychaudhuri et al (The Journal of Immunology, 139(1):271-278, 1987).

The claims have been described supra.

Oosterwijk et al teach a monoclonal antibody G 250 (Mab G 250) that reacts with a renal cell carcinoma antigen, G 250 antigen. The G 250 antigen is also expressed in several other tumor types (see Figure 3). As evidenced by Uemura et al the G 250 antigen is identical to MN protein (also known as carbonic anhydrase IX; CA IX or CA9) (see page 744, left and right column) and Pastorek et al teach the MN protein sequence, which shares 100% amino acid identity with the disclosed MN polypeptide of SEQ ID NO:2 (see the sequence alignment attached to the back of this office action), which is encoded by SEQ ID NO:1. Oosterwijk et al do not specifically teach an anti-idiotype antibody to an antibody that specifically binds to an MN protein. This deficiency is made up for in the teachings of Raychaudhuri et al.

Raychaudhuri et al has been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen in view of Oosterwijk et al as evidenced by Uemura et al and Pastorek et al and in view of Raychaudhuri et al because Oosterwijk et al teach a monoclonal antibody G 250 (Mab G 250) that reacts with a renal cell carcinoma antigen, the G 250 antigen, which is expressed in several other tumor types as well (see Figure 3). As evidenced by Uemura et al the G 250 antigen is identical to MN protein (also known as carbonic anhydrase IX; CA IX or CA9) (see page 744, left and right column) and Pastorek et al teach the MN protein sequence, which shares 100% amino acid identity with the disclosed MN polypeptide of SEQ ID NO:2 (see the sequence alignment attached to the back of this office action), which is encoded by SEQ ID NO:1. Furthermore, it would have been obvious to one skilled in the art that the polynucleotide encoding the MN protein, which shares 100% amino acid identity with the MN protein encoded by instantly claimed SEQ ID NO:1 would hybridize to the complement of SEQ ID NO:1 under the claimed stringent conditions. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an anti-idiotype antibody to an antibody that specifically

binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen in view of Oosterwijk et al as evidenced by Uemura et al and Pastorek et al and in view of Raychaudhuri et al because Raychaudhuri et al teach that immunization with anti-idiotype antibodies of the beta type (i.e., $Ab_2\beta$), bearing the internal image of a tumor antigen, induces tumor-specific immunity and can inhibit tumor growth. Thus, it would have been obvious to one skilled in the art to have produced an anti-idiotype antibody to an antibody that specifically binds an MN protein or polypeptide for treatment of human tumors expressing the MN tumor antigen in view of Oosterwijk et al as evidenced by Uemura et al and Pastorek et al and in view of Raychaudhuri et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at (571) 272-0827 from 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571) 272-0871.

Official papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published

in the Official Gazette, 1096 OG 30 (November 15, 1989). The official fax number for Group 1600 where this application or proceeding is assigned is (703) 872-9306.

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER